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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,175	09/23/2003	Nicole Zitzmann	080618-0304	1693

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EXAMINER	
BROWN, TIMOTHY M	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,175	ZITZMANN ET AL.	
	Examiner	Art Unit	
	Timothy M. Brown	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-45,47,49-55 and 58-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-45,47,49-55 and 58-66* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/04; 10/13/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Final Office Action is responsive to the communication received December 6, 2005. Claims 42-45, 47, 49-55 and 58-66 are pending.

Abstract

The abstract is objected to for being ungrammatical. Line 5 recites "may be contacting with a test compound . . . ." Having the abstract recite "contacted" would overcome this objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42, 45, 47, 49-55, 58, 60-66 are rejected under 35 U.S.C. 112, first paragraph because undue experimentation would be required to practice the full scope of the claims. Undue experimentation is defined by the following factors: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

In the present case, the claims recite "[a] method of screening for an inhibitor of HCV p7 protein comprising incorporating a p7 protein into a membrane" and contacting the membrane

with a test compound. The claims therefore include screening for HCV p7 inhibitors by contacting non-HCV p7 proteins, such as BVDV p7, with a test compound. However, the specification does not teach that BVDV p7 can function as a screening agent for HCV p7 inhibitors. The state of the art at the time of filing similarly fails to show that the HCV and BVDV p7 proteins are similar in structure and function such that an inhibitor of one protein would interact similarly with the other. In fact, little was known about the HCV p7 protein at the time of Applicants' filing.[1] Structural and conformational differences between the BVDV and HCV p7 proteins also suggest that the proteins' modes of activity may be different. Not only are the BVDV and HCV p7 proteins different sizes (70 and 63 amino acids respectively), they also have different amino acid compositions.[2] This difference is significant because it would produce different secondary structures and therefore require the inhibitors to have different interaction mechanisms. Therefore, it was entirely unclear whether the BVDV p7 protein could be used to predict the effect of a compound on HCV p7 permeability.

The content of the specification does not overcome this lack of predictability. The specification only discloses the sequence of the p7 protein and an assay for detecting the effect of candidate compounds on HCV p7 permeability. It does not teach a structural/functional relationship that is common to both p7 proteins such that one skilled in the art would have a reasonable expectation of success using BVDV p7 to screen for inhibitors of HCV p7. Therefore, one skilled in the art would have to invest significant research in defining the

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[1] De Francesco, R. "Biochemical and immunologic properties of the nonstructural proteins of the hepatitis C virus: implications for development of antiviral agents and vaccines" *Semin. Liver Dis.* 2000; 20 (1): 69-83 (citing abstract only).

[2] Griffin, S.D.C. "A conserved basic loop in hepatitis C virus p7 protein is required for amantadine-sensitive ion channel activity in mammalian cells but is dispensible for localization in mitochondria" Journ. Gen. Virol. 2004; 85: 451-461

functional regions of HCV p7, as well as the modifications that preserve the protein's activity. Accordingly, identifying HCV p7 inhibitors based on non-HCV p7 proteins would require undue experimentation.

Regarding claims 42-45, 47, 50-55, 58-61 and 63-66, the specification also fails to enable a method for screening for an inhibitor of HCV p7 protein comprising "***contacting one or more components of the p7-containing membrane with a test compound*** . . . ." The breadth of this language provides that the test compound may be contacted with only the membrane and not the p7 protein itself. However, the state of the art is such that determining whether a compound has an effect on a selected protein at least requires the compound to have an opportunity to contact, and interact with, the selected protein. One skilled in the art could not begin to predict how to measure a compound's effect on a protein without allowing the protein and compound to interact. Accordingly, developing a screening method for identifying HCV p7 inhibitors without allowing a test compound to interact with the p7 protein would require undue experimentation. Amending claims 42 and 58 with the following language would overcome this ground of rejection: "contacting the incorporated p7 protein with a test compound . . . ."

Regarding claims 42, 43, 45, 47, 49-55, 58 and 60-66, the specification fails to enable a screening method for identifying "an inhibitor of HCV p7 protein, comprising incorporating a p7 protein into a membrane . . . ." The breadth of this language allows the claims to read on screening for HCV p7 inhibitors by contacting a candidate compound with a portion of, or modified, p7 protein. Research subsequent to Applicants' filing date shows that using just a portion of the p7 protein would not provide a functional screening assay; the ion channel activity of HCV p7 depends on the conservation of a basic loop between two trans-membrane alpha

helices.[3] Thus, one skilled in the art could not easily predict how to screen for inhibitors using a non-wild type HCV p7 protein. The content of the specification does not overcome this problem because it only teaches using full-length p7 (e.g. Example 2.2). The specification also fails to detail the regions or motifs that must be conserved in order to maintain p7 function. Thus, the skilled artisan would have to invest significant experimentation by mapping the functional regions and permissive modifications that allow HCV p7 to retain its channel activity. Accordingly, identifying HCV p7 inhibitors using a non-full-length HCV p7 protein would require undue experimentation. Note that this reasoning also applies to claims 47 and 61. That is, undue experimentation would be required to modify the transmembrane domain as provided in these claims. This is especially true given that HCV p7's transmembrane domains are critical to its channel activity.[4]

Response to Arguments

35 U.S.C. 112, second paragraph

The rejection of claims 42-55 as being indefinite is withdrawn in view of Applicants' amendment.

35 U.S.C. 112, first paragraph

Claims 42-55 were rejected as non-enabled because the specification did not enable a method for identifying HCV antiviral agents. This ground of rejection has been withdrawn in view of Applicants' amendment and remarks.

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[3] Id.
[4] Id.

The rejection of claims 42-55 for lacking adequate written description is withdrawn in view of Applicants' amendment.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

i. Carrere-Kremer, S. "Subcellular localization and Topology of the p7 Polypeptide of Hepatitis C Virus" *J. Virol.* April 2002; 76 (8): 3720-3730

ii. Griffin, S.D.C. "The p7 protein of hepatitis C virus forms an ion channel that is blocked by the antiviral drug, Amantadine" *FEBS Letters* 2003; 535: 34-38

iii. Rowlands et al. WO 2004/005333 A1: Use of Hepatitis C Virus (HCV) P7 Protein

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

tmb

James C. Housel 2/20/06

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TMB 1/28/06